Neurobiological and Clinical Consequences of Stress

From Normal Adaptation to Post-Traumatic Stress Disorder

Editors

Matthew J. Friedman, M.D., Ph.D.
Professor, Departments of Psychiatry and Pharmacology
Dartmouth Medical School
Hanover, New Hampshire; and
Executive Director
National Center for Post-Traumatic Stress Disorder
Veterans Administration Medical Center
White River Junction, Vermont

Dennis S. Charney, M.D.
Professor and Associate Chairman for Research
Department of Psychiatry
Yale University School of Medicine
New Haven, Connecticut; and
Chief, Psychiatry Service
National Center for Post-Traumatic Stress Disorder
Veterans Affairs Medical Center
West Haven, Connecticut

Ariel Y. Deutch, Ph.D.
Associate Professor, Departments of Psychiatry and Pharmacology
Yale University School of Medicine
New Haven, Connecticut; and
National Center for Post-Traumatic Stress Disorder
Veterans Affairs Medical Center
West Haven, Connecticut

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Psychophysiological Evidence for Autonomic Arousal and Startle in Traumatized Adult Populations

*Annabel Prins, †Danny G. Kaloupek, and †Terrence M. Keane

*Department of Psychology, *Smith College, Northampton, Massachusetts 01060; and †Tufts University School of Medicine, National Center for Post-Traumatic Stress Disorder, Boston Veterans Affairs Medical Center, Boston, Massachusetts 02130*

The psychological impact of severe trauma, especially combat trauma, has a long literary, clinical, and scientific history (1,2). Clinically recognized combat syndromes such as irritable heart syndrome, shell shock, operational fatigue, and combat exhaustion have each included changes in physiological functioning as central to the syndrome (2). Similarly, noncombat syndromes like schreckneuroses following natural disasters (3) and railroad spine following life-threatening transportation accidents (4) have also included changes in somatic and autonomic activity as key features. More recently, psychophysiological changes associated with rape-trauma syndrome have been reported (5). Indeed, a close examination of all of these trauma syndromes reveals important similarities with regard to symptoms of autonomic hyperarousal (e.g., sleep disturbance, irritability, hypervigilance, and exaggerated startle responses). Today, these cardinal features of trauma are retained in the D symptom cluster of Post-Traumatic Stress Disorder (PTSD).

Until recently, physiological reactivity to reminders of the trauma was also included in the hyperarousal symptom cluster of PTSD. In DSM IV, this symptom has been moved to the reexperiencing symptom cluster because of its phasic features shared with the symptom of psychological distress following trauma-related cues (6). This change in emphasis is consistent with contemporary views of human stress responses that emphasize the importance of stressor meaning in mediating psychophysiological reactivity (7).

Psychophysiological studies of stress responses in humans, particularly those with PTSD, can be distinguished from other biological studies of stress by their reliance on noninvasive measurement procedures. Typically, bioelectrical signals generated from the body are conducted by surface electrodes and transducers. The signals are then filtered, amplified, and recorded for later interpretation of their biological or psychological significance. Biological interpretations tend to reflect a pathophysiological approach (8) where the underlying biological processes are thought to have direct or primary causal significance for the disorder. Psychological interpretations, on the other hand, tend to focus on the associations between physiological activity and psychological events or processes. This psychophysiological approach (8) is reflected in the majority of studies that have examined physiological changes after trauma-relevant stimuli in individuals with PTSD. Conversely, the pathophysiological approach is more commonly reflected in studies that have examined exaggerated startle responses in individuals with PTSD.

In addition to examining phasic responses to trauma-relevant stimuli and startle probes, psy-

chophysiological studies of PTSD have examined baseline differences between individuals with and without the diagnosis. The measures most frequently examined include: electrodermal activity, especially skin conductance (SC) levels and responses; heart rate (HR); systolic and diastolic blood pressure (BP); electromyographic (EMG) activity of the frontalis, corrugator, zygomaticus or orbicularis oculi muscles; and skin temperature. Several studies have attempted to identify physiological markers that relate to the diagnosis, while others have used psychophysiological measures as dependent variables to document treatment effectiveness (9,10,11,12). Thus, psychophysiological measures can facilitate diagnosis, provide measures of hyperarousal and reactivity that do not rely on self-report, and supply useful information for evaluating treatment effectiveness.

As a caveat, we note that psychophysiological assessment often has an elevated image as an objective means for detecting an individual's true psychological state. This is in part due to the use of polygraphy in forensic settings for lie detection. It is important to counteract this misconception by pointing out that psychophysiological measurement is only one of several methods for studying the nature of disorders such as PTSD. It can provide some unique information, at one level of scientific analysis, but it is not inherently more valid nor objective than other methods. On the other hand, psychophysiological methods are well suited to the investigation of autonomic hyperarousal and exaggerated startle in PTSD.

In this chapter, we will first review laboratory studies that have presented representations of traumatic events to adults with and without PTSD. Neither biological challenge studies nor studies that have examined the psychophysiological impact of talking about a trauma will be covered. However, in keeping with the theme of this book, we will examine potential differences in baseline levels of arousal and psychophysiological responding to other types of laboratory stressors. This broader evidence is important because it offers a perspective on two competing hypotheses. Specifically, it can help differentiate between the hypothesis that PTSD is characterized by biological changes that cause sustained increases in autonomic nervous system (ANS) activity, and the hypothesis that PTSD is characterized by psychological changes that lead to reactive increases in ANS activity only when trauma-relevant stimuli are encountered.

For the purposes of the review, physiological activity will be characterized as autonomic activity even though the effects in question might be due to sympathetic activation, parasympathetic withdrawal, or both. Psychophysiological studies of PTSD have not addressed this distinction and, in fact, most do not even appear to recognize that these two ANS branches have independent and complementary effects, as well as their better-known reciprocal effects (13). Our review will focus on HR and SC because they are the most widely used measures of general ANS activity and appear to be the best discriminators between individuals with and without the PTSD diagnosis (14,15).

Finally, we will consider the literature on exaggerated startle responses in adults with and without PTSD. We will focus on orbicularis oculi EMG activity and eyeblink responses because the startle reflex is principally skeletomuscular in nature. Secondarily, the ANS measures of HR and SC will be examined as adjunctive indices of arousal. Following this review, we will address the need to consider individual differences in reactivity, as well as situational and methodological variables influencing psychophysiological responding in future research on the psychophysiology of PTSD.

EMPIRICAL STUDIES INVOLVING EXPOSURE TO TRAUMA-RELATED AND GENERIC STRESSORS

Research on the psychophysiology of trauma appeared in the literature as early as the 1940s with Kardiner (16), who observed that individuals with "chronic war neurosis" were particularly sensitive to stimuli associated with the original trauma and reacted to these stimuli with distinctive patterns of psychophysiological responding. Gillespie (17) also observed increased tonic levels of muscle tension and palpitations

in traumatized war veterans. These clinical impressions were later corroborated by controlled laboratory studies.

Tonic differences in arousal were documented by Wenger (18), who found that 225 patients diagnosed with "operational fatigue" demonstrated higher resting heart rates and SC levels as compared with 98 "psychoneurotics" and 448 control subjects. Dobbs and Wilson (19) were the first to conduct a controlled experiment on psychophysiological responses to combat sounds. Eight "decompensated" WWII veterans were compared with 13 "compensated" WWII veterans (i.e., with no signs of psychiatric impairment) and 10 noncombat control subjects. Consistent with the findings of Wenger, Dobbs and Wilson found higher mean baseline HR in both the compensated (78.3 bpm) and decompensated (79.4 bpm) groups as compared with the control group (66.5 bpm). Although measurement artifact due to behavioral agitation in the "decompensated" subjects prevented meaningful comparisons involving their data, Dobbs and Wilson also found statistically greater increases in HR during exposure to combat sounds for the "compensated" group (M=6.1 bpm) as compared to the non-combat controls (M=2.5 bpm).

To date, the majority of studies on the psychophysiology of trauma have employed Vietnam combat veterans as subjects. This may be due to the unique availability within the Veterans Administration (VA) system of large numbers of individuals who have suffered similar traumas, as well as the need for the VA to provide comprehensive assessments for individuals seeking compensation for psychiatric disability. More recently, similar assessment protocols have been applied to other trauma groups (e.g., sexual assault survivors, motor vehicle accident victims) with comparable success.

Psychophysiological assessments typically begin with a resting baseline period, the duration of which has varied across studies from 30 seconds (following a 3-minute relaxation tape) to 30 minutes. Tonic levels of arousal are usually obtained during this period. Next, the subject is exposed to either neutral (e.g., music) or trauma-related stimuli. Assessment stimuli have been presented in one of three ways[1]. Some researchers have used audiotapes of neutral or trauma-relevant sounds, while others have employed visual images (i.e., slides and film) with an accompanying sound track. Still others have presented subjects with scripts describing neutral and idiographic trauma-related experiences. Most often these scripts are read to subjects who are instructed to imagine the scene as clearly and vividly as possible.

The duration of exposure to neutral and trauma-related stimuli also has varied from one 30-second period to 30 minutes. Although within-subject psychophysiological reactivity is most frequently expressed as a difference score from an immediately preceding baseline, in several studies the psychophysiological reactivity index has been defined more conservatively by determining the difference between presentation periods for the trauma-related stimuli and the neutral stimuli. Exposure to generic (i.e., not related to trauma) stressors such as mental arithmetic or imagery with nontraumatic content has also been included in some protocols as an additional source of within-subject comparison. Most often, the between-group comparison involves psychophysiological responses of PTSD subjects relative to a similar group of trauma survivors without PTSD.

BASELINE LEVELS OF AUTONOMIC AROUSAL

Group comparisons with respect to baseline levels of arousal are presented in Table 1. Significant differences in baseline heart rate were reported in 5 out of the 13 studies summarized. The PTSD group had higher resting heart rate than the non-PTSD group in all five studies. Only one study reported significant differences in baseline SC levels (21), and in this instance

[1]A fourth type of trauma-related stimulus presentation was recently reported by McCaffrey et al. (20). These investigators found significant electroencephalogram (EEG) changes following exposure to trauma-related odors (e.g., odors simulating burning flesh) in five Vietnam veterans with PTSD as compared with five Vietnam veterans without PTSD. Unfortunately, McCaffrey et al. (1993) did not collect data on either HR or SC.

TABLE 1. *Baseline levels of heart rate, skin conductance and subjective distress in PTSD*

Study	Groups	Baseline length	Baseline skin conductance	Baseline heart rate	Power	Baseline subjective distress
Blanchard et al. (23)	1. VN–PTSD (11) 2. Non-vets–NMD (11)	10-minute adaptation + 10-minute baseline	values not reported - ns[a]	1. 77.5 2. 70.2*[b]	.39[c]	not collected
Malloy et al. (26)	1. VN–PTSD (10) 2. VN–NMD (10)	5-minute baseline	SC values not obtained	1. 94.0 (15.3) 2. 84.5 (17.2) ns[d]	.35	not reported
Pallmeyer et al. (37)	1. VN–PTSD (12) 2. VN–NMD (10)	12-minute adaptation + 2-minute baseline	values not reported	1. 81.0 (10.7) 2. 69.5 (10.6)*[d]	.79	not collected
Blanchard et al. (110)	1. VN–PTSD (57) 2. VN–NMD (34)	12-minute adaptation + 2-minute baseline	values not reported	1. 78.8 (14.6) 2. 65.2 (12.7)*[d]	1.00	not collected
Pitman et al. (15)	1. VN–PTSD (18) 2. VN–NMD (15)	3-minute relaxation + 30-second baseline	1. 1.45 (1.0) 2. 1.34 (0.6) ns	1. 75.3 (10.6) 2. 66.3 (8.5)*[d]	.84	not reported
Gerardi et al. (111)	1. VN–PTSD (18) 2. VN–Non-PTSD (18)	~8-minute adaptation + 10-minute baseline	1. .22 (.12) 2. .15 (.14) ns[d]	1. 76.1 (15.5) 2. 63.0 (13.9)*[d]	.83	not collected
Blanchard et al. (94)	1. VN–PTSD (59) 2. VN–NMD (12)	12-minute adaptation + 2-minute baseline	values not reported	1. 72.9 (12.9) 2. 63.3 (11.3) ns[e]	.79	not collected
McFall et al. (22)	1. VN–PTSD (10) 2. mixed non-PTSD (11)	30-minute rest + 30-minute baseline	not collected	1. 63.2 (2.2) 2. 63.5 (3.5) ns[f]	.08	negative affect: (0–68 scale) 1. 12.1 (3.1) 2. 4.7 (1.1)*[f]
Pitman et al. (24)	1. VN–PTSD (7) 2. VN–other anxiety disorders (7)	3-minute relaxation + 30-second baseline	1. 2.8 (4.1) 2. 2.6 (2.8) ns	1. 70.8 (12.0) 2. 73.6 (7.9) ns	.12	not reported
Orr et al. (30)	1. WWII + Korean veterans - PTSD (8) 2. WWII + Korean veterans–Non-PTSD (12)	3-minute relaxation + 30-second baseline	1. 2.6 (1.9) 2. 3.5 (2.7) ns	1. 71.6 (12.2) 2. 71.8 (11.7) ns	.05	not reported
			Other Trauma			
Shalev et al. (21)	1. non-veteran - PTSD (13) 4♀, 9♂ 2. non-veteran - Non-PTSD (13) 7♀, 6♂	3-minute relaxation? + 30-second baseline	1. 4.7 (2.8) 2. 6.7 (2.0)* (opposite direction)	1. 73.2 (12.9) 2. 77.7 (13.1) ns	.22	not reported
Orr & Pitman[†]	1. childhood sexual assault (20, ♀) 12 current full PTSD; 8 past full PTSD 2. childhood sexual assault - Non-PTSD (13, ♀)	3-minute relaxation + 30-second baseline	1. 3.0 (2.6) 2. 4.3 (3.5) ns[d]	1. 73.9 (9.3) 2. 71.8 (9.8) ns[d]	.15	not reported
Blanchard et al. (31)	1. MVA PTSD (23) 2. MVA non-PTSD (17)[g]	7-minute adaptation + 5-minute baseline	values not reported	1. 70.2 2. 72.0 ns[c,h]	.12	not reported

Non-PTSD=Comparison group includes some subjects with nonpsychotic Axis I disorders.

[a]There was a nonsignificant group X condition interaction.

[b]Original values and significance reported in Blanchard et al. (110).

[c]The standard deviations used for this power analyses was 12.0. Our one-tail *t* test for independent groups was nonsignificant.

[d]Original values obtained from authors (Special thanks to Robert Gerardi and Scott Orr).

[e]A significance test was not conducted in the original study. Our one-tail *t* test for the independent group was significant.

[f]An average of four samples from baseline period (0, 10, 20, and 30 minutes) was used. The negative affect score was obtained from a composite of 17 adjectives (e.g., disgust) placed on a five point scale.

[g]No information on number of male and female subjects in each group was provided.

[h]No information on standard deviations was provided. Original values were obtained from figures in the text.

*$p<0.05$.

[†]Unpublished paper presented by Orr and Pitman at the 1993 annual meeting of the International Society for Traumatic Stress Studies, San Antonio, Texas.

MVA, motor vehicle accident; NMD, no mental disorder; PTSD, post-traumatic stress disorder.

the PTSD group had *lower* SC levels than the non-PTSD group. The one study that reported on baseline levels of subjective distress (22) found significant differences in negative affect during a 30-minute baseline period, with the PTSD group reporting more distress than the non-PTSD group.

Because it appeared that significant findings in baseline arousal might be related to sample size, we conducted independent one-tailed *t* tests and power analyses for each study. When exact values were not reported, we relied on figures and graphs to estimate baseline HR and SC values. The results of our analyses are provided in Table 1 along with the significance reported by the original investigators. Our analyses suggest that when the power of a study was relatively high (i.e., greater than .75) reliable differences were evident; when power was low (i.e., less than .40), however, the reported differences were not reliable.

Notably, baseline differences in HR are only evident in early studies on combat-related PTSD. More recent studies on both combat and non-combat-related PTSD do not find sustained differences in arousal. Several explanations can be offered to account for the apparent downward shift in baseline levels of arousal for combat-related PTSD, as well as the nonsignificant findings of more recent nonveteran PTSD studies:

1. Many of the early studies on combat-related PTSD employed comparison groups of non veterans (23) or veterans without a mental disorder. These studies were the most likely to find significant differences in baseline levels of arousal. When trauma survivors with other Axis I psychiatric disorders are used as a comparison group, differences in baseline levels of arousal are noticeably reduced. For example, Pitman and colleagues (24) found that Vietnam veterans with other anxiety disorders had slightly *higher* baseline HR than Vietnam veterans with PTSD. Thus, reported differences in baseline levels may be a function of the comparison group used, with higher tonic levels of arousal perhaps being characteristic of anxiety disorders in general (25).
2. Those studies using shorter baselines tended to report greater HR variability and higher baseline values. For example, the highest HR values for both the PTSD and non-PTSD groups were reported by Malloy et al. (26), who employed a baseline duration of only 5 minutes. On the other hand, the lowest HR values with the least variability was reported by McFall et al. (22), who used a 30-minute baseline period preceded by a 30-minute period of adaptation and rest. Indeed, with the exception of the McFall et al. study (22), the so-called baseline period in all of these studies is less than what would be required to index basal physiological states. Recommendations about baseline length by Hastrup (27) point to a minimum of 15 minutes for studies that examine psychophysiology in relation to acute laboratory stressors. The shorter baseline levels in most existing PTSD studies are, therefore, best understood simply as reference levels of ANS arousal under conditions of relatively diminished ambient stress.
3. Although psychophysiological procedures involving exposure to feared cues has become standard in the assessment of anxiety disorders (25), many of the early PTSD studies employing such procedures were met with skepticism and concern regarding subject welfare. In order to obtain approval for these studies, informed consent and procedural instructions often included demand characteristics that may have contributed to elevated levels of arousal. For example, subjects in the Malloy et al. (26) study were instructed "not to push [themselves] to the limit" and to "stop if the scenes become upsetting." Subjects in the Blanchard et al. (23) study were asked after each phase if they wanted to continue. The possibility of a demand characteristic influencing arousal is partially supported by the high degree of escape behavior observed in early studies on the psychophysiology of PTSD (25) as compared to later studies.
4. Relatedly, baseline differences in arousal may be confounded by anticipatory anxiety, given that these values are typically col-

TABLE 2. *Psychophysinogical reactivity and subjective distress following exposure to trauma-related and trauma-unrelated laboratory stressors*

		Trauma				Other stressors			
Study	Groups	Exposure duration and reactivity defined	Skin conductance reactivity	Heart rate reactivity	Subjective distress	Exposure duration and reactivity defined	Skin conductance reactivity	Heart rate reactivity	Subjective distress
Auditory stimuli									
Blanchard et al. (23)	1. VN PTSD (11) 2. Non-Vets–NMD (11)	≤5 trials: 30 seconds per trial; last combat phase–last music phase	not reported–ns[a]	1. 9.1 2. −1.6*[b]	not collected	not specified: mental arithmetic–preceding baseline	not reported–ns[a]	1. 6.5 2. 6.0 ns[c]	not collected
Pallmeyer et al. (37)	1. VN PTSD (12) 2. VN NMD (10)	≤5 trials: 30 seconds per trial; last combat phase–last music phase	not reported	1. 5.4 2. −0.2*[b]	not collected	not specified: mental arithmetic–preceding baseline	not reported	1. 5.2 2. 7.0 ns[c]	not collected
Blanchard et al. (110)	1. VN PTSD (57) 2. VN NMD (34)	≤5 trials: 30 seconds per trial; last combat phase–last music phase	not reported	1. 10.6 2. 3.5*[c]	not collected	not specified: mental arithmetic–preceding baseline	not reported	1. 6.1 2. 8.2 ns[c]	not collected
Gerardi et al. (111)	1. VN PTSD (18) 2. VN non-PTSD (18)	≤5 trials: 30 seconds per trial; last combat phase–last music phase	not reported–ns[a]	1. 9 2. −1*[c]	not collected	not specified: mental arithmetic–preceding baseline	not reported–ns[a]	1. 8 2. 9 ns[c]	not collected
Blanchard et al. (94)	1. VN PTSD (59) 2. VN NMD (12)	≤5 trials: 30 seconds per trial; last combat phase–last music phase	not reported	1. 3.5 2. 0.25*[c]	not collected	not specified: mental arithmetic–preceding baseline	not reported	1. 6.0 2. 9.0*[c]	not collected
Audio-Visual stimuli									
Malloy et al. (26)	1. VN PTSD (10) 2. VN NMD (10)	≤9 scenes: 60 seconds each; combat scenes–neutral scenes	SC values not obtained	1. 11 2. −0.5*[c]	fear thermometer (0–11 scale) 1. 4.8 2. 2.2*[c]	not collected	not collected	not collected	not collected

McFall et al. (22)	1. VN PTSD (10) 2. mixed non-PTSD (11)	10-minute VN video; comat–preceding baseline	not collected	1. 6.8 (1.8) 2. 1.1 (1.4)*	Negative Affect: (0–68 scale) 1. 23.7 (3.7) 2. 5.5 (0.3)*	10 minute MVA video: MVA–baseline	not collected	1. 1.6 (1.0) 2. 1.6 (1.3) ns	1. 10.2 (2.1) 2. 3.8 (1.8)*
Idiographic stimuli									
Pitman et al. (15)	1. VN PTSD (18) 2. VN NMD (15)	2 × 30-second trauma imagery: imagery–preceding baseline	1. 0.6 (0.6) 2. 0.05 (0.15)*[c]	1. 5.78 (5.5) 2. 3.0 (4.0) ns[c]	Valence Pleasantness: (0–12 scale) 1. 0.6 (0.9) 2. 1.9 (1.5)* Arousal 1. 10.7 (1.2) 2. 10.0 (1.9) ns	A. 30-second precombat trauma imagery script–preceding baseline B. 30-second public speaking fear script–preceding baseline	A. not reported–ns B. 1. 0.0 2. not reported–ns	A. not reported–ns B. 1. 1.7 2. not reported–ns	A. valence and arousal not reported–ns B. valence and arousal not reported–ns
Pitman et al. (24)	1. VN PTSD (7) 2. VN other anxiety disorders (7)	2 × 30-second trauma imagery: imagery–preceding baseline	1. 0.50 (0.45) 2. 0.10 (0.18)*[c]	1. 5.75 (5.5) 2. 3.0 (2.5) ns[c]	Valence Pleasantness: 1. 0.4 (0.9) 2. 2.7 (2.1)* Arousal: 1. 11.2 (1.2) 2. 7.9 (2.3)*	A. 30-second precombat trauma imagery script–preceding baseline B. 30-second public speaking fear script–preceding baseline	A. not reported–ns B. not reported–ns	A. not reported–ns B. not reported–ns	A. not reported B. not reported
Orr et al. (30)	1. WWII + Korean War PTSD (8) 2. WWII + Korean War non-PTSD (12)	2 × 30-second trauma imagery: imagery–preceding baseline	1. 1.1 (1.1) 2. 0.05 (.25)*[c]	1. 9.9 (8.0) 2. 1.5 (1.5)*[c]	Valence Pleasantness: 1. 0.4 (0.4) 2. 0.6 (1.0) ns Arousal: 1. 10.6 (1.6) 2. 10.3 (2.1) ns	A. 30-second precombat trauma imagery script–preceding baseline B. 30-second public speaking fear script–preceding baseline	A. 1. 0.2 (0.4) 2. 0.1 (0.4) ns B. 1. −0.1 (0.3) 2. 0.0 (0.2) ns	A. 1. 6.4 (7.9) 2. 1.0 (3.1)* B. 1. 2.7 (4.9) 2. 2.0 (3.1) ns	not reported
Shalev et al. (21)	1. non-veteran PTSD (13) 4♀ 9♂ 2. non-veteran non-PTSD (13) 7♀ 6♂	30-second trauma imagery: imagery–preceding baseline	1. 0.9 (1.2) 2. 0.3 (0.6) ns	1. 13.9 (10) 2. 2.0 (7.9)*	not reported	A. 2 × 30-second nontrauma stressors–preceding baseline B. 30-second dental fear script–preceding baseline	A. not reported–ns B. not reported–ns	A. not reported–ns B. not treated–ns	not reported
Orr & Pitman[f]	1. childhood sexual assault PTSD (20, ♀) 2. childhood sexual assault non-PTSD (13, ♀)	2 × 30-second trauma imagery script: imagery–preceding baseline	1. 0.72 (0.8) 2. 0.49 (0.7) ns[f]	1. 1.7 (1.9) 2. 0.6 (1.5)*[f]	not reported	30-second nontrauma stressor–preceding baseline	not reported	not reported	not reported

continued

TABLE 2. *Continued.*

Study	Groups	Trauma				Other stressors			
		Exposure duration and reactivity defined	Skin conductance reactivity	Heart rate reactivity	Subjective distress	Exposure duration and reactivity defined	Skin conductance reactivity	Heart rate reactivity	Subjective distress
Blanchard et al. (31)	1. MVA PTSD (23) 2. MVA non-PTSD (17)[g]	A. 2 × 3-minute idiographic trauma imagery: imagery–preceding baseline B. 3-minute MVA video: video–preceding baseline	not reported	Script #1 1. 5.7 2. 1.2**[e] Script #2 1. 2.2 2. −1.0**[g] MVA video 1. −0.2 2. −1.9 ns[c]	Script #1 1. 55 2. 30**[e] Script #2 1. not reported 2. not reported MVA video 1. not reported 2. not reported	3-minute mental arithmetic–preceding baseline	not reported	1. 6.9 2. 5.6 ns[c]	not reported

Non-PTSD=comparison group includes some subjects with nonpsychotic Axis I disorders.

[a]There was a nonsignificant group X phase interaction.

[b]Mean values were obtained from the Blanchard et al. (110) study. Information on standard deviations was not provided.

[c]Mean values were obtained from figures or tables in the text. Information on standard deviations was not provided.

[d]A significance test was not provided in the original study.

[e]Mean values and standard deviations were obtained from figures in the text.

[f]Values were obtained from authors (Scott Orr). Values are expressed as square root microvolts and square root beats per minute.

[g]No information on the number of male and female subjects in each group was provided.

*$p<0.05$.

[†]Unpublished paper presented by Orr and Pitman at the 1993 annual meeting of the International Society for Traumatic Stress Studies, San Antonio, Texas.

MVA, motor vehicle accident; NMD, no mental disorder; PTSD, post-traumatic stress disorder.

lected when subjects are anticipating exposure to trauma cues[2]. In a recent study that did not include exposure to trauma cues (28), 11 Vietnam combat veterans with PTSD were compared to 11 asymptomatic controls on several measures of basal sympathoadrenal function, including HR. Two to 4 weeks after participating in diagnostic and psychometric testing, these medication-free subjects were brought into the laboratory and placed in a supine position for 30 minutes prior to a 30-minute data collection period. The results showed that the PTSD subjects were not significantly different from control subjects on any measure. These investigators concluded that tonic sympathetic nervous system activity is not significantly elevated for patients with PTSD. Similar findings were reported by Shalev et al. (29) in their study on exaggerated startle responses in PTSD (see startle section). In this study, subjects with PTSD were no different than trauma survivors without a mental disorder on baseline HR, SC, and obicularis oculi EMG activity. Finally, support for an anticipatory effect confounding baseline differences in arousal comes from the one study that reported on baseline levels of subjective distress. As previously noted, PTSD subjects in the McFall et al. (22) study reported more preexposure subjective distress than the non-PTSD group.

PHASIC CHANGES IN AUTONOMIC AROUSAL

Group differences in reactivity to laboratory stressors which are both related to and unrelated to trauma are reported in Table 2. As with Table 1, when exact values were not reported, we used the figures in the text to estimate HR and SC reactivity. Because standard deviations were rarely provided, we were unable to compute independent t tests and power analyses for these studies. Significant differences in HR reactivity to trauma-relevant stimuli were reported in 11 of the 13 studies reviewed. Significant differences in SC levels or SC responses were found in three of the seven studies that provided information on this measure. Subjective ratings of distress are reported as absolute scores in Table 2 because baseline reference values were generally not collected. Of the six studies that reported subjective distress ratings, five found significant differences between the PTSD group and the non-PTSD group, with the PTSD subjects reporting more distress after the trauma-relevant stimuli than did the non-PTSD comparison subjects.

Only one study out of 11 (30) found significant differences in HR reactivity to generic stressors, while no studies found significant differences in SC to these stressors. The one study that included subjective distress ratings for the generic stressor (22) found that the PTSD group reported significantly more subjective distress than the non-PTSD group.

It seems safe to conclude that, at least for combat-related trauma, combat veterans with PTSD show significantly more psychophysiological reactivity to combat stimuli than various comparison groups (i.e., normal controls, nonveterans with other psychiatric diagnoses, combat veterans with no mental disorder). For HR, this reliable and robust finding held for all protocols that utilized standardized audio or audiovisual combat stimuli. Significant differences in SC were more common in assessments using idiographic imagery scripts, although HR differences were in the expected direction for these protocols as well. Despite the different scales used to assess subjective distress, Vietnam veterans with PTSD consistently reported more distress than Vietnam veterans without PTSD. Only the WWII and Korean War veterans with PTSD were not significantly different from WWII and Korean War veterans without PTSD on subjective ratings of distress (30).

[2]In a recently published paper by Gerardi et al. (112), 32 Vietnam veterans with PTSD were compared to 26 age-, race-, and sex-matched Vietnam era veterans with no combat experience on a number of physiological variables, including heart rate, while waiting in the admitting area of a large VA Medical Center. Thus, there was no expectation of exposure to combat cues. These authors found that the subjects with PTSD had higher "basal" heart rate levels than the matched controls.

Although the direction of psychophysiological responding in subjects with noncombat PTSD is similar to that observed in subjects with combat-related PTSD, several important distinctions are apparent:

1. The method of stimulus presentation in these studies has involved exposure to idiographic (trauma) imagery scripts. For combat-related PTSD, the presentation of idiographic scripts most clearly demonstrated differences with respect to SC responding. This does not seem to hold for noncombat PTSD. Blanchard et al. (31) used both standardized and idiographic trauma cues and found HR, rather than SC, to be the most reactive to the idiographic stimuli; the standardized stimuli did not produce significant differences in either HR or SC. Similar findings were reported by Shalev et al. (21), who found significant HR changes due to idiographic scripts but no significant changes in SC.
2. The magnitude and variability of responding to noncombat presentations may bear an inverse relationship to the duration and frequency of exposure to the trauma-relevant stimuli. For example, Shalev et al. (21) exposed subjects to one 30-second trauma-relevant imagery script. Although the HR changes associated with this script were considerably higher than those reported in other studies, the degree of variability was also much greater.
3. Studies on noncombat-related PTSD have included female subjects in contrast to the exclusive use of male subjects in studies of combat veterans. It is too early to tell how psychophysiological responding is influenced by gender. In the one study that directly examined gender differences in civilian trauma (21), female subjects with PTSD demonstrated 33% greater physiological responding to their trauma script than male subjects with PTSD. More specific information about gender differences in HR or SC was not provided, and the small number of subjects in the study made the observed differences nonsignificant.

Consistent with the findings from combat-related PTSD, psychophysiological responding does not appear to generalize to generic laboratory stressors. This interpretation is reinforced by intrasubject comparisons of responses to trauma-related and generic laboratory stressors, which indicate that the psychophysiological reactivity seen in PTSD is specific to the trauma-relevant material. Such response specificity supports a classical conditioning model of PTSD (32,33), but additional research is needed to explain the observed discordance found by Orr (30) between self-reports of distress and physiological responding to trauma-related stimuli. At present this discordance does not appear to be unique to PTSD, because it is also found in relation to generic stressors (22,30).

EXAGGERATED STARTLE RESPONSE

Despite self-reports of exaggerated startle in PTSD (34) and standardized procedures for evoking startle responses in humans (35), only a few studies have examined this symptom of PTSD in the laboratory. The protocols used to assess startle responses in PTSD have typically involved exposure to acoustic startle probes, although these probes have varied in frequency, intensity, duration, and rise and fall times. The aspects of startle most frequently reported in these studies include magnitude of responding to an unwarned signal and trials to nonresponse (i.e., habituation). Table 3 provides a review of the published studies on this topic.

As previously noted, startle is primarily a skeletomuscular response that can be easily indexed by eyeblink responses or orbicularis oculi EMG activity. Although three studies have used either of these measures to examine response magnitude or trials to habituation, only the Butler et al. study (36) found significant differences (in response magnitude) between the PTSD and non-PTSD groups. On the other hand, all three studies that used autonomic measures found significant differences in ANS activity, with the PTSD group showing greater SC and HR responding to the startle probes as compared with the control group.

TABLE 3. *Startle responses in PTSD*

Study	Groups	Startle probe	Startle responses	Measures	Findings
Pallmeyer et al. (37)	1. VN PTSD (12) 2. VN NMD (10)	1 × 80 dB, 2000 msec, burst white noise, ? rise time	A. magnitude	HR; change score from baseline	A. *Magnitude* 1. 1.25 2. −1.5*[a]
Ross et al. (34)	1. VN PTSD (9)[b] 2. Non-Vets NMD (9)	150 × 100 dB [SPL], 1000 hz, 50 msec, <1 msec rise and fall time	A. trials to habituation	eyeblink amplitude	A. *trials to habituation* 1. 15 2. 25 ns
Butler et al. (36)	1. VN PTSD (13) 2. VN NMD (12)	6 × 40 msec noise burst at 85, 90, 95, 100, 110, and 116 dB[A].	A. magnitude	right orbicularis oculi EMG response; transformed digital units (1 unit=15 microvolts)	A. *magnitude*[a] −85 dB 1. 2.5 2. 2.0 ns −90 dB 1. 7.5 2. 2.0 ns −95 dB 1. 15.0 2. 2.0* −100 dB 1. 20.0 2. 5.0* −110 dB 1. 32.0 2. 15.0 ns −116 dB 1. 43.0 2. 25.0 ns
Paige et al. (42)	1. VN PTSD (12) 2. VN NMD (6)	4 × 780 hz tone, 500 msec duration at 74, 84, 94, and 104 dB[SPL] with 25 msec rise and fall times	A. magnitude	EEG (not reviewed here) HR	A. *magnitude*[a,c] −74 dB 1. 2.6 2. 2.5 −84 dB 1. 2.6 2. 1.3 −94 dB 1. 2.9 2. 0.5 −104 dB 1. 3.7 2. 1.7
Shalev et al. (29)	1. mixed trauma PTSD (14) 11♂, 3♀ 2. trauma NMD (15) 10♂, 5♀	15 × 95 dB[SPL], 1000 hz, 500 msec tone, 0 msec rise and fall times	A. magnitude B. trials to habituation	left orbicularis oculi EMG response, SC response, HR response; (square root transformations)	A. *magnitude*[d] −*EMG* *1. 0.9 (0.8)* *2. 0.4 (0.5) ns* −*SC* *1. 0.77 (0.37)* *2. 0.29 (0.16)** −*HR* *1. 2.7 (1.6)* *2. 1.5 (0.9)** *B. trials to habituation* −EMG 1. 9.1 (5.9) 2. 5.9 (5.1) ns −SC 1. 13.1 (3.2) 2. 6.3 (5.0)* −HR 1. not reported 2. not reported

[a]Values were obtained from figures in the text.
[b]Only data from 7 PTSD patients were used in analyses.
[c]Statistical significance for each dB level was not provided. However, HR slope was significant.
[d]EMG, SC, and HR slopes were not significant.
*$p<0.05$.
NMD, no mental disorders; PTSD, post-traumatic stress disorder.

Of this set of studies, the one by Pallmeyer et al. (37) has features that may undercut its value in the context of startle testing. First, it is unclear whether the stimulus was powerful enough to elicit a startle response, because the intensity was near startle threshold (80–85 dB), and the absence of information about stimulus rise or fall times suggests that they were not carefully controlled. This is important because Blumenthal (38) has shown that responses to stimuli near the startle threshold are particularly affected by onset rise time. The possibility of insufficient potency is consistent with the finding that the non-PTSD control group showed a *decrease* in HR responding to the startle stimulus. Second, the startle stimulus was delivered within the context of an assessment that involved exposure to trauma cues, a factor that may have led to startle potentiation. Just as anticipatory anxiety may increase baseline levels of arousal, evidence based on non-PTSD subjects suggests that anticipatory anxiety can potentiate the startle reflex (39). Thus, even though the Pallmeyer et al. study did not conform to the temporal proximity between fear stimulus and startle probe often used in the fear-potentiated startle paradigm (40), the affective context of the study may have had a comparable excitatory effect (41).

The fact that the acoustic startle probes used by both Shalev et al. (29) and Paige et al. (42) would have sounded like gunfire adds to the possibility of inadvertent fear potentiation. These investigators have argued that their findings support the hypothesis that PTSD is associated with abnormalities in unconditioned responding. However, the validity of this assertion rests on the untested assumption that the startle probes did not have conditioned significance to the subjects. Although the nature of the trauma experienced by subjects in the Shalev et al. (29) study was not reported, subjects in the Paige et al. (42) study were Vietnam combat veterans whose trauma experiences probably included some form of exposure to gunfire. Given these considerations, differential responding to the startle probes may have reflected conditioned responding alone, or the impact of conditioned responding as a potentiator of unconditioned responding.

The possibility that loud tones may have conditioned relevance receives support from the Butler et al. study (36). These investigators examined responding to both acoustic and tactile startle probes. Despite significant differences in responses to the acoustic startle probe, PTSD and non-PTSD subjects showed similar responses to the tactile probes. Butler et al. suggest that these findings support a stimulus-specific increase in startle response for individuals with PTSD, and argue that this interpretation has "clinical appeal since many veterans report that auditory stimuli, such as an automobile 'backfire,' will result in an exaggerated startle" (36).

SUMMARY AND CONSIDERATIONS FOR FUTURE RESEARCH

Table 4 offers an interpretive summary of our findings. Our review of the psychophysiological evidence provides strong support for the exis-

TABLE 4. *Interpretive summary of psychophysiological evidence for autonomic arousal and startle responses in PTSD*

	Outcome measure			
Assessment period	Heart rate	Skin conductance	EMG	Subjective distress
Baseline[a]	+/−	−	NR	+
Trauma Reactivity	++	++	NR	++
Generic stressor Reactivity	−	−	NR	−
Acoustic Startle[b]	+	+	−	NR

++ clear positive association
+ probable positive association
+/− inconsistent findings
− probable negative association
−− clear negative association
EMG, electromyographic
NR, not reviewed

[a]See text for argument that elevated baseline levels of arousal may be a function of anticipatory anxiety related to forthcoming exposure to trauma cues in psychophysiological studies of PTSD.

[b]See text for argument that acoustic startle probes may have conditioned significance for combat veterans with PTSD.

tence of differentially greater ANS reactions when individuals with PTSD are exposed to trauma-related stimuli. Although ANS reactions can also be observed in response to laboratory stressors that are unrelated to trauma, our review suggests that the magnitude of this responding does not differ between individuals with and without the disorder. In addition, our review of potential basal differences in ANS arousal associated with PTSD suggests that observed differences in baseline levels are best understood as "elevations" linked to anticipatory "distress." We conclude that it is unlikely that stable elevations in ANS activation are characteristic of PTSD *in the absence of some proximal psychosocial cause.* The clinical reports of sustained elevations may be the result of more frequent triggering of affective states that provoke arousal in individuals who have been traumatized. However, this possibility has not as yet been addressed by research.

Our review of the startle research with PTSD populations suggests continuity with the evidence for psychophysiological reactivity. Differences in laboratory startle responding that are associated with PTSD status appear to be the result of fear potentiation of the response. This distinction is important because it emphasizes the role of the ambient emotional state rather than relying on a stable, biologically altered propensity to startle. We also note that the current set of positive startle findings with PTSD patients are based on the use of acoustic startle probes that may have affective relevance for the subjects as a result of their similarity to the sound of gunfire. For both of these reasons, we believe that the concept of conditioned fear may offer more explanatory power for the body of evidence than does the notion of biological alteration. While better understanding of the biological underpinnings of affective reactions will be a valuable element of our understanding of PTSD, current psychophysiological evidence points to the role of conditioned affective cues as a more critical focus at this time.

Beyond the literature review, the potential impact of anticipatory responding is also suggested by evidence that elevations in baseline arousal are associated with greater subsequent psychophysiological reactivity. Litz et al.[3] created groups of combat veterans on the basis of relative HR reactivity to combat audiovisual presentations and found that they differed rather dramatically in terms of resting HR values. Specifically, the more reactive veterans had resting values approximately 20 beats per minute higher than their less reactive counterparts. Assuming that the difference in resting values reflects anticipatory anxiety as we propose, it may be that this background state potentiates subsequent reactivity in a manner analogous to the effect that baseline arousal appears to have on the likelihood of panic attacks in response to challenge (e.g., lactate infusion (43)). This pattern may be related to a broader psychophysiological phenomenon with respect to HR, for which *between-groups* evidence indicates a consistent positive relationship between baseline values and the magnitude of reactivity (44).

The unique psychophysiological response pattern shown by PTSD subjects following trauma cues has been observed in diverse traumatized populations using a variety of stress-inducing stimuli. In a few instances, the pattern of response has been used to statistically discriminate them from both asymptomatic and psychiatric control subjects. These discriminant function analyses using psychophysiological variables have correctly classified PTSD subjects and their non-PTSD counterparts from 80% to 100% (45). However, these overall hit rates do not reflect the consistent finding that specificity (i.e., percentage of non-PTSD subjects correctly classified) is better than sensitivity (i.e., percentage of PTSD subjects correctly classified). In fact, the sensitivities of discriminant function equations have ranged from 61% to 91%, while specificities have ranged from 86% to 100% (46). These findings indicate that as many as 40% of patients with PTSD do not demonstrate the expected psychophysiological reactivity. Interestingly, Butler et al. (36) reported that a similar percentage of PTSD subjects were not

[3]Unpublished paper presented by Litz, Forsyth, Kaloupek, and Slavkin at the 1991 annual meeting of the Association for the Advancement of Behavior Therapy, New York, New York.

responsive to startle probes. This lack of consistency in responding is an important target for future investigation. What follows is discussion of several factors that may account for the psychophysiological nonresponsiveness of some individuals with PTSD.

Violations of the Boundary Conditions of Assessment

First, the integrity of the assessment procedure must be considered. Valid physiological data can be obtained only if certain boundary conditions are met. As with computerized axial tomography (CAT) scans that require patients to be motionless during the procedure, psychophysiological assessments typically place restrictions on the amount of movement subjects can display while data are collected. They also require compliance with task demands that involve viewing, imagining, and/or listening to material that can evoke strong emotional reactions. Instructions or other constraints may be used to counteract the self-protective or self-regulating tendencies that most individuals are likely to manifest under these circumstances. However, because the emotional reactions are aversive, efforts to limit processing of the stimuli (e.g., turning away from slides or curtailing images) or regulate arousal (e.g., deep breathing) are still common. Unfortunately, when boundary conditions are violated in these ways, physiological systems are subject to influences that can generate or dampen ANS arousal in a manner difficult to quantify (47). Thus, it is understandable that response patterns associated with the PTSD diagnosis are not uniform.

Behavioral agitation often observed during assessment is meaningful as an index of emotional distress and should be given particular consideration in clinical evaluations. However, unless special care is taken in the placement of transducers (e.g., electrodes), movement can easily become so extreme that recordings are infeasible, as was observed in the "decompensated" group in the Dobbs and Wilson (19) study. Moreover, less extreme motoric activity caused by emotional distress may result in elevations of psychophysiological responding, particularly cardiovascular responding. In keeping with our earlier discussion of the autonomic factors that underlie some of the measured physiological reactions, it should be noted that such cardiac-somatic coupling is more likely to reflect the withdrawal of parasympathetic influences rather than the increased activation of sympathetic influences (48). The importance of this distinction for PTSD is not currently clear.

Variables that affect physical state may also challenge the boundary conditions for assessment. Factors such as time of day (i.e., circadian phase) and laboratory temperature or humidity are given some consideration in the assessment of PTSD, but it is still typical for them not to be rigorously controlled. On the other hand, numerous extraneous influences are not easily controlled and can acutely disrupt psychophysiological recording. Among these influences are speaking, coughing, fidgeting, changes in breathing pattern, emotional thoughts unrelated to the procedure (e.g., about a prior argument with a spouse), and physical discomfort from a variety of sources (e.g., uncomfortable seating position, full bladder). Within broad limits, these may not be a major problem *as long as the effect of interest is robust.* In addition, many of these potential problems can be minimized by careful planning and preparation of the physical environment where measurement takes place. Control of the psychological and behavioral influences that might confound the emotional targets of interest also can be managed through the study design and procedures.

More difficult to manage is the uncontrolled use of medications by patients, as well as the consumption of caffeine and nicotine by many research subjects prior to psychophysiological testing for PTSD. The unfortunate fact is that there is not much empirical literature to help disentangle the impact of medications from other influences contributing to the observed response patterns. Psychoactive drugs aimed at anxiety or depression are probably most relevant for PTSD research, and available data indicate that some of these medications reduce both HR and SC activity (49). Drugs with clear autonomic effects (e.g., beta blockers) pose an even greater

problem because their impact is likely to be substantial, but there is no available adjustment for psychophysiological data. For example, it is not possible to specify a dose-related formula for adjusting the responding of medicated subjects so that the unmedicated equivalent of their responding can be estimated.

The use of nicotine and caffeine can also have pronounced influence on the physiological systems that are typically monitored in PTSD studies. Unfortunately, their effects are neither uniform across physiological systems nor solely tied to consumption. Nicotine produces cardiovascular effects in the form of increased HR, as well as increased systolic and diastolic blood pressure (BP) (50). The effects of nicotine on HR appear to be additive with the effects of stress (51), and interactive with depression and trait anxiety (52). Furthermore, withdrawal from nicotine decreases HR and SC responses, while increasing subjective anxiety, depression, and irritability that may affect behavior during assessment (53,54). Finally, nicotine may act in combination with oral contraceptives to have an enhanced impact on BP during stress (54), warranting particular attention to these factors when young women are tested.

Caffeine also has cardiovascular effects, but the effect on HR is apparently minimal in comparison to the effect on BP (55,56). This effect may be particularly pronounced for individuals who have a family history that places them at risk for hypertension (57). As with nicotine, caffeine withdrawal is associated with irritability and discomfort (58). However, some evidence indicates that anxiety, depression, and hostility can be increased by moderate-to-high acute doses (59). Given this evidence, the fact that use—even heavy use— of these substances is very common in veterans with PTSD (60) makes their potential impact all the more noteworthy for the existing (and future) literature on the psychophysiological assessment of PTSD.

Limitations of Physiological Measures

There are also some problematic features of the measures used to reflect ANS activity. A basic concern is the differential sensitivity that measures appear to have with respect to psychological or behavioral influences. Theory, empirical evidence, and working experience with these measures all indicate that tasks that evoke states such as attention, vigilance, active avoidance, or inhibition of ongoing behavior are better indexed by some physiological systems than by others—and even by some components of systems rather than by others (61,62,63). As an example, active avoidance appears to have primary impact on the cardiovascular system. Thus, consideration must be given to the features of any psychophysiological assessment task when measures are being selected or, conversely, the task must be constructed so as to capitalize on the strengths of available measures.

Another important limitation is that there are no noninvasive measures that provide a direct, error-free index of ANS activity. One strategy for overcoming this problem is to use convergent data from two or more measures to create an index of ANS reactivity. We are currently investigating the use of concurrent HR and SC increase as such a convergent index for PTSD assessment. We make the assumption that both measures reflect some common aspects of the sympathetic arousal linked to PTSD, as well as their own unique sources of autonomic effects and error. Two indices are created to reflect: (1) from among the sample points during a measurement period that shows HR increase, the proportion that shows concurrent SC increase, and (2) from among the sample points that show SC increase, the proportion that shows concurrent HR increase. In principle, these convergent indices should offer greater sensitivity and validity than single system indices currently used for PTSD assessment (64).

Limitations of Diagnostic Methods

The diagnostic interviews and psychometric instruments typically used as criteria for PTSD diagnosis are subject to several sources of error. At minimum, the current methods are nondiscriminating with regard to factors such as patient motivation (e.g., compensation seeking) that

may lead to false positive case identification. Another broad possibility is that these methods—or perhaps even the DSM diagnostic system on which they are based—may be overinclusive (65). One aspect of the problem is that the multiple symptom options available under the diagnosis of PTSD make it possible to obtain a diagnosis of PTSD without the presence of psychophysiological reactivity. The fact that psychophysiological reactivity is not isomorphic with the disorder means that the absence of this symptom may reflect a particular subtype of PTSD. If so, the reactivity could have implications for predicting treatment response to both pharmacological and nonpharmacological interventions (c.f. 66,67) or, in a more proactive sense, for serving as a basis for treatment matching (c.f. 68,69). It could also be the case that the diagnostic system should be less flexible with regard to the necessity of this symptom (70).

Finally, it is important to recognize that the foundation of the PTSD diagnosis is subjective information not necessarily comparable to information recorded directly from physiological systems. Evidence from research on autonomic perception and response covariation (71,72,73) makes it clear that self-reports of psychophysiological reactivity are not interchangeable with observations or recordings of such activity. Thus, reports of physiological reactivity or startle are not likely to show high consistency with more direct measures of these phenomena, or at least are not likely to do so for many individuals. A related point about self-report assessment is that not all formats are equivalent. Evidence indicates that subjective ratings of distress that are in a dimensional format (e.g., those anchored to arousal or valence) correlate more highly with psychophysiological measures than do ratings anchored to affective states such as distress or anxiety (74).

Uncontrolled Variation in Individual Biological Influences

Individual differences that can influence psychophysiological reactivity arise from intrinsic subject variables such as age, sex, race, menstrual cycle, and physical fitness level. These variables are rarely considered in psychophysiological research on PTSD, but their relationship to sustained and reactive features of ANS activity has been established in other studies employing psychophysiological methods.

Epidemiological and laboratory studies have shown that HR both at rest and in response to various laboratory stressors tends to decrease with age, while BP levels and reactivity tend to increase (75,76,77). Recent evidence broadens the implications of these trends by showing that chronic stress and social support are possible moderators of these changes (78).

Differences between races and genders have been found with respect to HR, BP, and SC measures in a number of studies (79,80,81,82). Black subjects have generally demonstrated lower HR and SC levels, and higher BP levels and reactions to stress than white subjects. Furthermore, the two races seem to differ in the behavior of these measures during physical stress (e.g., cold pressor (83)) and in relation to psychosocial variables (e.g., depression and anger (84)), thereby complicating data interpretation.

Gender differences in response to laboratory stressors generally indicate greater BP reactivity for men and greater HR reactivity for women. In addition, there appear to be differences across phases of the menstrual cycle that need to be considered whenever premenopausal women are tested (85,86). Finally, there is a mixture of positive and negative findings concerning reductions in physiological response to stressors as a function of both aerobic fitness levels and acute exercise (87,88,89,90,91). Despite the lack of consistent findings, there is no question that sustained and acute physiological adjustments to exercise can be substantial for both men and women. Accordingly, exercise-related information may be important to the interpretation of psychophysiological data from PTSD assessments.

Individual differences in the primary physiological channels of affective response expression, a phenomenon related to the general psychophysiological principle of individual response stereotypy (92), may also contribute to the im-

pression that reactivity is inconsistent across PTSD subjects. For example, some individuals may respond to emotional stimuli primarily with HR changes, while others may respond mainly with SC changes; still others may express physiological reactivity in channels other than HR or SC. As one means for addressing this issue, Levis and Smith (93) have suggested that an individual's dominant response channel can be determined by an independent "biological" stress test, such as a balloon-burst. In their sample of 39 students, significant response consistency was shown between this procedure and a psychological stressor for subjects who were classified as high responders in a given channel. Of course, this approach is limited by the degree to which the number of different physiological responses being monitored covers the range of primary channels for the individuals being assessed.

Each of the previously noted factors is of sufficient strength to affect the relationship between psychophysiological measures and clinically relevant stimulus conditions such as presentations of trauma cues. However, this evidence applies only to visceral responding. Factors such as race and gender are generally treated as random error rather than being subjected to analysis as independent variables in studies that address the motor response of startle (i.e., eyeblink). As a result, there is little evidence available concerning their potential impact in this context.

Uncontrolled Variation in Individual Psychosocial Influences

Experiential and developmental factors such as degree of trauma exposure, presence of comorbid disorders, and patterns of coping also complicate the measurement and interpretation of psychophysiological data. Only a few studies have examined the relationship between experiential factors such as degree of combat exposure and psychophysiological reactivity to trauma cues, or response to startle probes. Although several investigators have failed to find a relationship between combat exposure and psychophysiological reactivity (15,94), Orr et al. (95) found that group differences in HR response to trauma cues were substantially reduced when anxious subjects were matched for combat exposure with PTSD subjects. Given that magnitude of psychophysiological reactivity may be related to event severity, subjects may need to be matched on this dimension when there is concern about separating the effects of trauma exposure from those of the PTSD syndrome per se. A similar suggestion was made by Butler et al. (36) with regard to relationship between combat exposure and startle.

Other forms of psychopathology often accompany PTSD, particularly depression, anxiety, and substance abuse (96,97). Evidence from other areas suggests that these conditions may have an impact on efforts to distinguish psychophysiological (or startle) responders from nonresponders as a function of changes they cause in HR, SC, and facial EMG activity (98,99,100). The evidence is mixed with regard to PTSD research. Pitman et al. (15) found no difference between PTSD subjects diagnosed as having or not having major depression in terms of their physiological reactivity. However, Orr et al. (95) found that depression at the symptom level as measured by the Beck Depression Inventory (BDI) was positively correlated with reactivity. Conversely, Litz et al.[4] found that HR responders (with increases $\geq$7 bpm following combat slides/sounds) were less depressed in terms of the Minnesota multiphasic personality inventory depression (MMPI-D) scale than were HR nonresponders. Blanchard et al.(94) found no significant differences between responders and nonresponders on either the BDI or MMPI-D.

Psychophysiological responding will depend in part on the way the assessment is appraised by the subject, learned patterns of coping (e.g., self-regulatory behaviors) they bring to the assessment procedure, and opportunities available for coping before and during the procedure. For example, Lader (101) found dramatic decreases

[4]Unpublished paper presented by Litz, Weathers, Kaloupek, Gerardi and Keane at the 1990 meeting of the Association for the Advancement of Behavior Therapy, San Francisco, California.

in ANS arousal during dissociation in patients with severe anxiety. In a more controlled study, Bloom et al. (47) demonstrated that attention diversion during laboratory stress tasks can reduce physiological reactivity. Such efforts to limit processing of stimulus presentations can be viewed as potentially meaningful indicators of distress, but they are more difficult to manage insofar as their threat to the validity of psychophysiological data. Just as there may be a reciprocal relationship between avoidance and arousal/distress as hallmark symptoms of PTSD, it can be difficult to determine whether the absence of arousal and distress during a psychophysiological assessment is the result of successful efforts to limit processing of the stimulus presentations or simply is due to lack of affective relevance. Part of the complication is that many of the maneuvers that subjects use to distance themselves from evocative stimuli are not readily identified by observation or other external monitoring.

While creative efforts to measure avoidance behavior in the context of assessment are needed, at minimum subjects might be given a retrospective opportunity to report on their behavior during the assessment, with particular emphasis on behaviors likely to alter their physiological reactions to the stimulus presentations. Although there are not as yet any formal means for incorporating this information into the scoring of the psychophysiological data, it does provide a basis for eliminating data segments of questionable validity. Perhaps it will eventually be possible to develop ways to use the information to quantify the relative amount of functional stimulus contact that occurred during the procedure, and then to adjust the psychophysiological reactivity index accordingly. Currently, this goal is far from realization.

ADDITIONAL METHODOLOGICAL CONSIDERATIONS

There are at least three additional features of the methods used for psychophysiological assessment that deserve scrutiny because of their potential to influence the quality and interpretation of the resulting data.

The Functional Impact of Laboratory Stressors

Obrist (48) identified a distinction among laboratory stressors that is potentially important for the design and interpretation of psychophysiological studies of PTSD. He proposed, and subsequent research has tended to support his hypothesis, that tasks involving active coping will engage the cardiovascular system more than tasks involving passive coping. By definition, active coping involves effortful attempts to influence task outcome (102). For example, it is elicited by mental arithmetic, cognitive problem solving, and interpersonal influence tasks. In contrast, passive coping is not effortful or aimed at influencing outcome. It is elicited by tasks such as watching a film or engaging in imagery, which primarily involve passive sensory intake. The majority of studies on PTSD have presented trauma-related stressors in the context of tasks that would engage passive coping although, as indicated earlier, the actual nature of task-related coping may be more complex than expected.

These considerations also apply to the evaluation of response to startle probes. In line with the preceding discussion, these probes may be experienced as aversive and subjects may make efforts to reduce their impact. This may be particularly the case when warning signals are delivered prior to the probes. It may be more difficult for subjects to make acute adjustments to moderate the aversiveness of unsignaled probes, but this difficulty may merely lead to more sustained strategies for disengaging from the task. In any case, the critical point is the importance of recognizing both the formal features of the tasks and their functional impact when the resulting psychophysiological data are being interpreted.

The Content Relevance of Trauma Cue Presentations

The relative strengths and weaknesses of standardized and idiographic approaches to trauma cue selection need to be considered. The primary advantage of a standardized presentation is its uniformity and potential for allowing tight ex-

perimental control. The primary disadvantage is a potentially limited range of application. For example, presentations suitable for veterans are not likely to be suitable for victims of motor vehicle accidents or crime. Conversely, a primary advantage of idiographic scripts is the potential for making comparisons across different trauma populations. The key to such comparisons is development of a standardized protocol for selecting the material for presentation. The investigator must be able to match presentations across individuals in terms of important conceptual (as opposed to concrete) features. Examples of such features might include portrayal of physical threat, description of a subjective sense of extreme fear, helplessness, or horror, and reference to bodily reactions triggered by the depicted situation. A related advantage is that idiographic presentations may closely approximate the internal (memory) representations of the traumatic experience and thereby improve the validity of assessment. Potential disadvantages of idiographic scripts are primarily due to the use of imagery as the typical format for their presentation. This approach is hampered by the need to accommodate individual differences in the ability to engage in imagery and difficulties related to monitoring task compliance. Admittedly, this latter consideration is only marginally easier to deal with when the presentations are in an audiovisual format. In general, the selection of format will depend upon the priorities and aims of the professionals who conduct the assessment. Thus far, the most direct comparison of formats to be published (31) suggests that the idiographic approach generates more consistent response differences linked to PTSD.

Precision and Timing of Measurement Collection

The majority of published studies have quantified psychophysiological variables so as to reflect relatively extended (e.g., 30 or 60 seconds) recording intervals. Many studies further aggregate the information by averaging over two or more intervals. These methods are suited to empirical questions that concern relatively stable responding throughout an interval, or responding that is subject to significant error in measurement. However, the benefits of aggregation are realized at the cost of sensitivity and may not be optimal for the purposes of PTSD assessment. Empirical evidence from Orr et al.[5] and Blanchard et al. (31) indicates that averaging across two trauma presentations can result in diluted findings. In addition, earlier findings reported by Malloy et al. (26) indicate that most significant physiological responding can occur during exposure to one particular slide in a series of presentations. Therefore, quantification approaches that aim to identify peak intervals for reactivity may offer greater sensitivity and perhaps even better matches with evidence provided by nonphysiological sources (e.g., interviews or self-ratings).

Similarly, it is important to either measure during temporal intervals that are most likely to show responding, or to use methods that identify peak reactivity within longer intervals. Identification of critical measurement windows is most easily explained in the context of startle studies, because the effects are phasic and short-lived. Roth et al. (103) have provided empirically based guidelines for optimal measurement intervals for startle response—intervals that have not been consistently used in PTSD startle studies. Presentations of trauma relevant cues typically are not subject to the same level of specification regarding optimal responding, at least in part because of the uncontrolled individual differences that affect responding. This problem can be overcome by identifying response peaks within the presentation period. Consider, for example, the impact that coping efforts are likely to have on HR responding during a 1-minute trauma-relevant presentation. Initial reactivity followed by disengagement from the task can produce distinctly high and low values in the same interval, leading to an aggregate value that is potentially indistinguishable from that produced by an interval during which the rate was steady at a moderate level. However, the physiological data will better reflect the psychological character of the intervals if peak response is identified.

[5]Unpublished paper presented by Orr and Pitman at the 1993 annual meeting of the International Society for Traumatic Stress Studies, San Antonio, Texas.

TRENDS AND SUGGESTIONS

Addressing the Emotional Specificity of Psychophysiological Findings

To date, most of the research on the psychophysiology of PTSD has focused on establishing the diagnostic and discriminant validity of the disorder without considering the meaning of the psychophysiological responding. Discriminant validity is an empirically determined quality that is not tied to biological or psychological significance. For example, it may be that psychophysiological responding is closely tied to changes in mood state, but this relationship would be overlooked because almost all of the research has used PTSD diagnosis as the primary independent variable rather than attempting to address the mediating influences more directly.

Several investigators have found that emotions other than fear (e.g., anger) are differentially elicited for PTSD and non-PTSD groups following exposure to trauma cues (15,24). The ANS reactivity can be associated with emotional states other than anxiety, and response differences between different emotions are difficult to detect using peripheral ANS measures such as HR and SC (104). However, there is a growing body of evidence that emotion-specific responding is reflected in patterns of facial muscle contraction (105,106). Future studies using facial EMG may help to elucidate the emotional networks activated during exposure to trauma cues.

Evaluating Recovery of Responding

An approach that has been fruitful with regard to other psychophysiological research, including research on anxiety disorders (107), is examination of response recovery. This approach is based in part on the recognition that responding to stressors has adaptive value and, as appears to be the case for generic stress tasks, may not be differentially affected by diagnostic status. The maladaptive aspects of the responding may be evident in the period after the stressor ends, as indexed by elevations in ANS activity that persist despite the absence of provocation. A number of the important aspects of this approach have been outlined by Haynes et al. (108).

Ambulatory Monitoring

Ambulatory assessment has been conducted with respect to other anxiety disorders, most notably panic disorder, with some success (109). Similar methods may be valuable for PTSD for at least three reasons.

1. Ambulatory monitoring may help resolve the issue of the origins of resting elevations in physiological measures associated with the condition. Orr (personal communication, February 28, 1994) and his colleagues have already used 24-hour ambulatory measurement to test for differences in HR between individuals with and without PTSD. Their initial findings indicate no stable differences, consistent with our view that resting differences prior to assessment are the result of anticipatory distress.
2. In psychometric terms, ambulatory measurement can help to establish the ecological validity of laboratory-based psychophysiological assessments by quantifying the relationship between reactivity in the lab and in the natural environment.
3. More important, ambulatory measurement would allow direct measurement of the magnitude of responding in natural settings where patients are confronted with unexpected reminders of their traumatic events.

As has been shown with panic disorder patients, information gained from ambulatory monitoring can contribute to both clinical care for individuals and increase theoretical understanding of the condition in general.

CONCLUSIONS

Finally, two points in conclusion. First, Anderson and McNeilly (79) have persuasively argued that a contextual approach to psychophysiological research is needed. According to this perspective, psychophysiological responding is

a function of the ecological niche that the person inhabits at the time of assessment. This point seems particularly appropriate for psychophysiological testing conducted with individuals who have experienced traumatic stress. Their behavior may be determined by and reflective of heightened sensitivity to physical threat. This outlook can be expected to influence their perceptions of and behavior in the assessment environment.

Second, despite the long list of factors that can complicate the use of psychophysiological measures in PTSD research, some consistent findings do emerge. Our hope is that future refinements in the selection and application of psychophysiological measures will enhance their value to both clinical and research efforts with traumatized populations.

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